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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/021,368	12/12/2001	Vimla Band	00398-100005	3165

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EXAMINER	
NASHED, NASHAAT T	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/021,368	BAND, VIMLA	
	Examiner	Art Unit	
	Nashaat T. Nashed, Ph. D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *69-75 and 82-99* is/are pending in the application.

4a) Of the above claim(s) *96-99* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *69-75 and 82-95* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The application has been amended as requested in the communication of June 23, 2004. Accordingly, claims 69 and 75 have been amended, claims 76-81 have been canceled, and new claims 82-99 have been entered. New claims 84-95 are directed to a diagnostic method, which involves whether NES1 gene in a biological sample has a mutation, and new claims 96-99 are directed to a kit comprising wild-type human NES1 nucleic acid sequence. The method of new claims 84-95 are distinct from those of claims 69-83 as the two methods have different steps. Since examining the two independent methods represents no search burden on the examiner, the two methods are examined together. In contrast, the subject matter of claims 96-99 is new in this application, and is subjected to restriction requirement from the pending methods claims. The kit comprising the nucleic acid encoding NES1 is related to the pending method as a product and a method of use. Since the nucleic acid of the kit can be utilized in other methods such as in a method to make NES1 protein, the restriction between the method and the product is proper. The restriction is made FINAL.

Claims 69-75, and 82-95 are pending.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 69-75, and 82-95 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 and 10-14 of U.S. Patent No. 6,153,387 (387') for the reasons set forth in the prior Office action, mailed December 19, 2003.

Applicants have not presented any argument against the above rejection.

New claims 82 and 83 are included in this rejection because they are drawn to the same method and their embodiments are covered by the method of claim 10. New claims 84-95 (method-II) are directed to a diagnostic method similar to that of claims 69-75, 82, and 83 (method-I). The two methods differ in their third step of the method. Step 3 of method-I is a quantitative measurement of the expression product (either protein or nucleic acid) of the NES1, and compare the result to that of a control experiment. In contrast, step 3 of method-II involve the isolation of a nucleic acid and determine its sequence to identify mutation. Thus, isolating the nucleic acid in method I and determining mutation in the nucleic acid would be an obvious variation of method I, and therefore, claims 84-95 are included in this rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 69-75, 82-93, and 95 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons set forth in the prior Office action mailed December 19, 2003.

In response, applicants limited the method claim to human gene and biological sample from human, and argue that they have disclosed the human gene NES1 having the nucleic acid sequence of SEQ ID NO: 2.

Applicant's arguments filed June 23, 2004 have been fully considered, but they are found unpersuasive. The claims are not limited to the human NES1 gene of which SEQ ID NO: 2 is a cDNA product. The specification defines NES1 polypeptide as:

> By "NESI polypeptide" is meant an amino acid sequence, which is a cell cycle-regulated serine protease whose expression negatively correlates with the presence of malignant epithelial cells. Preferably, such a polypeptide has an amino acid sequence, which is at least 45%, preferably 60%, and most preferably 85% or even 95% identical to the amino acid sequence of the NESI protein of Fig. 10 (SEQ ID NO: 1)", see the paragraph bridging pages 6 and 7.

From the above genus of nucleic acid encoding NES1 polypeptide, only the species of SEQ ID NO: 2 is described. While the methods claimed are limited to human NES1 gene and the biological sample is from human, one of ordinary skill in the art would still

recognize that applicant has not fully described the entire genus of the NES1 genes. To overcome the above rejection, the claim must contain a structural feature of the NES1 gene accompanied by a functional feature. New claims 82-93 and 95 are included in this rejection because the NES1 gene is not defined by structural and functional features.

Claim 69-75, 82-93 and 95 are rejected under 35 U.S.C. 112, first paragraph, for lack of enablement for the reasons set forth in the prior Office action mailed December 19, 2003.

Applicants argue that the claims as amended are enabled by the specification as filed.

Applicant's arguments filed June 23, 2004 have been fully considered, but they are not deemed to be persuasive. Enablement requires a disclosure sufficient to allow a person of skill in the art to practice the full scope of the claimed invention without undue experimentation. The previous Office action sets out a *prima facie* case of non-enablement, explaining by sound scientific reasoning why a person of ordinary skill in the art would doubt that the guidance of the specification would enable practice of the full scope of the claimed invention without undue experimentation. Applicants have presented no evidence or, indeed, any arguments to establish the adequacy of the disclosure to enable the scope of the instant claims. Applicants merely assert that the disclosure of NES1 of SEQ ID NO: 2 is sufficient enablement for the claimed method as amended. Although the specification teaches the cDNA of SEQ ID NO: 2, it does not even teach the human NES1 gene, i. e., the genomic DNA. The specification defines NES1 polypeptide as:

> By "NESI polypeptide" is meant an amino acid sequence, which is a cell cycle-regulated serine protease whose expression negatively correlates with the presence of malignant epithelial cells. Preferably, such a polypeptide has an amino acid sequence, which is at least 45%, preferably 60%, and most preferably 85% or even 95% identical to the amino acid sequence of the NESI protein of Fig. 10, see the paragraph bridging pages 6 and 7.

Thus, the examiner assumes that NES1 gene would be any human gene which encodes a polypeptide having at least 45% identity to the amino acid sequence of SEQ ID NO: 1, and is a cell cycle-regulated serine protease whose expression negatively correlates with the presence of malignant epithelial cells. Applicants make no effort to explain why they consider the disclosure of a cDNA of SEQ ID NO: 2 would enable the scope of the claimed methods as defined above. Conclusory statements unsupported by evidence or scientific reasoning are insufficient to overcome the *prima facie* case of non-enablement set out in the previous Office action. New claims 82-93 and 95 are included in the above rejection because they have the same scope of the originally claimed method.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 84-95 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

(a) The clauses "wherein a mutation in the sequence indicates that the human ....." in claim 84, and "wherein the mutation is relative to the sequence of SEQ ID NO: 2" in claim 94 render the claims indefinite because the resulting claims do not clearly set forth the metes and bounds of the patent protection desired. Silent mutation, noncoding region of SEQ ID NO: 2, or those resulting of a conserved amino acid substitution would not be expected to have a significant diagnostic value. Thus, including these embodiments in the method claims render the method inoperable.

(b) The phrase "or altered binding or cleavage activity" in claim 91 renders the claims indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. The amplified NES1 sequence is a nucleic acid sequence and it is not clear from the claim or the specification to what the amplified nucleic acid sequence binds or what activity does have.

(c) Claims 85-90, 92, 93 and 95 are included in this rejection because they are dependent on a rejected claim and do not cure its deficiencies.

No claim is allowed.

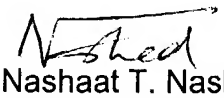
Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is 571-272-0934. The examiner can normally be reached on MTTF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Nashaat T. Nashed, Ph. D.
Primary Examiner
Art Unit 1652